Supplemental Figure Legends

Supplemental Figure 1. The designer proteins ZF-552SKD, ZF-598SKD, and ZF-4203SKD down-regulate SOX2 protein levels in MDA-MB-435s **(A)** and MCF7 **(B)** cells. **(A)** SOX2 protein down-regulation quantified from the signal intensities of the SOX2-specific bands as assessed by western blot (**Figure 2B**) in MDA-MB-435s. Cells were transduced with either empty vector, ZF-552SKD, ZF-598SKD, ZF-619SKD or ZF-4203SKD. As positive control for the knowck-down, the same cells were transfected with a siRNA specific for *SOX2*. The Mock sample refers to non-transfected cells. Bands were quantitated using imageJ 1.45 software and normalized to empty vector control. **(B)** SOX2 protein down-regulation in MCF7 cells. Cells were stably transduced with either empty vector, with ZF-552SKD or ZF-598SKD expressing constructs. The ATFs were induced upon treatment with Doxycycline (+Dox). The signal intensities of the SOX2-specific bands from western blots (**Figure 2D**) were quantitated as described above.

Supplemental Figure 2. Quantification of *SOX2* mRNA in MCF7 cells after treatment with 5-aza-2'-deoxycytidine (5-Aza) analysed by qRT-PCR. MCF7 cells were stably tranduced with either empty vector, ZF-552SKD or ZF-598SKD. Cells were either un-induced or treated with Dox (+Dox). These cells were simultaneously either vehicle-treated or treated with 5-Aza (5 μM). Cells were collected and processed for the detection of *SOX2* mRNA by qRT-PCR. Data were normalized to empty vector-transduced cells.

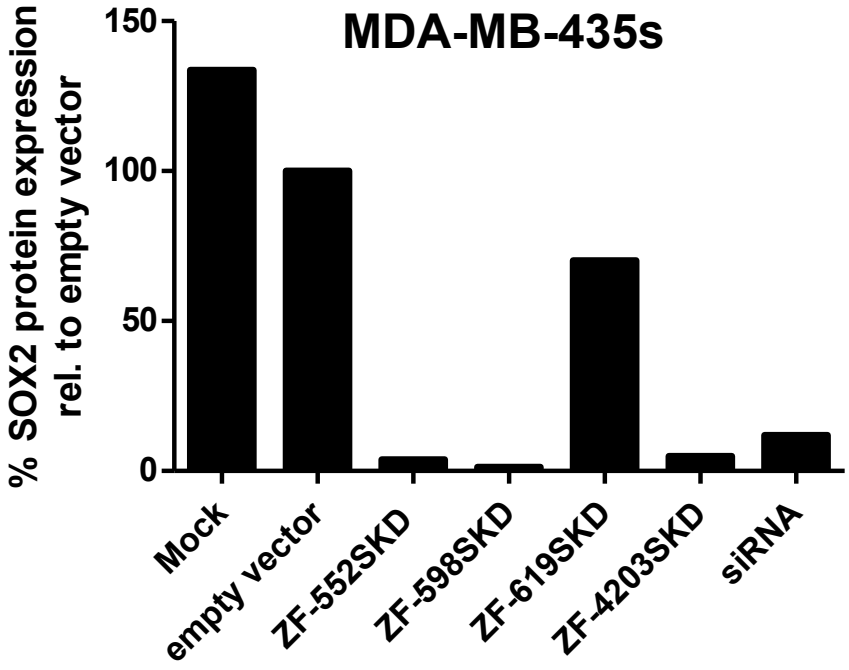
Supplemental Figure 3. The designer ZF silencers down-regulate *Cyclin D1* mRNA expression. Quantification of *Cyclin D1* mRNA expression in MCF7 was analysed by qRT-PCR. MCF7 cells were stably transduced with either empty vector, ZF-552SKD or

ZF-598SKD. The ATFs were induced with Doxycyclin (+Dox) and the expression levels of *Cyclin D1* were quantified and normalized to empty vector-transduced cells; * $p<0.05$.

Supplemental Figure 4. The *SOX2* cDNA rescues the growth inhibitory phenotype of the designer ZF silencers. MCF7 cells stably transduced with ZF-552SKD or ZF598SKD were infected with lentiviral supernatants generated from control empty vector (control) or exogenous *SOX2* cDNA (pSin*SOX2*, Addgene). 48 hours post-infection, the ATF expression was induced with Doxycycline (+Dox) and the cell culture density of the plates was examined 72 hrs post-induction. Pictures were taken at 40x magnification.

Supplemental Figure 1

A



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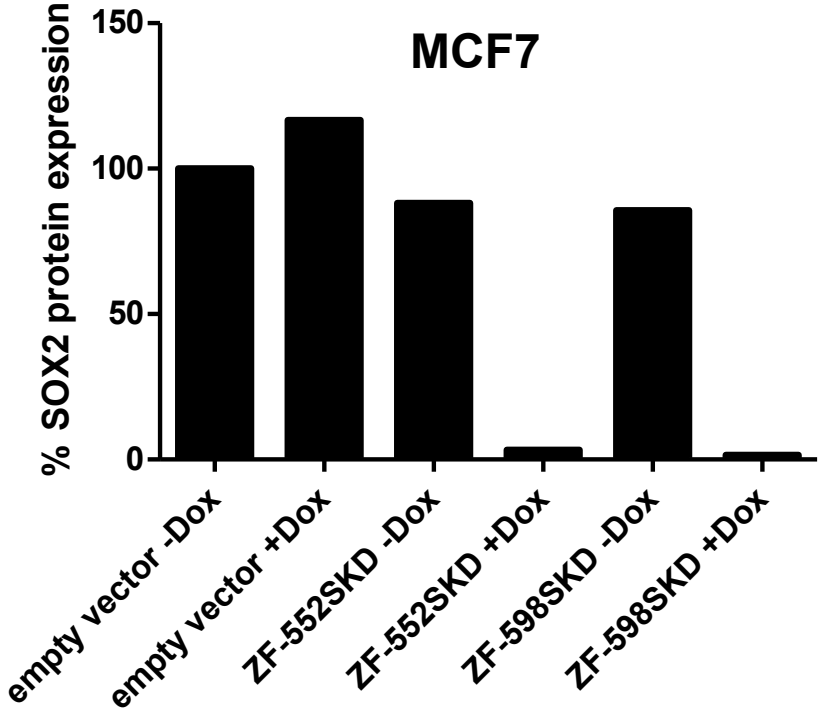
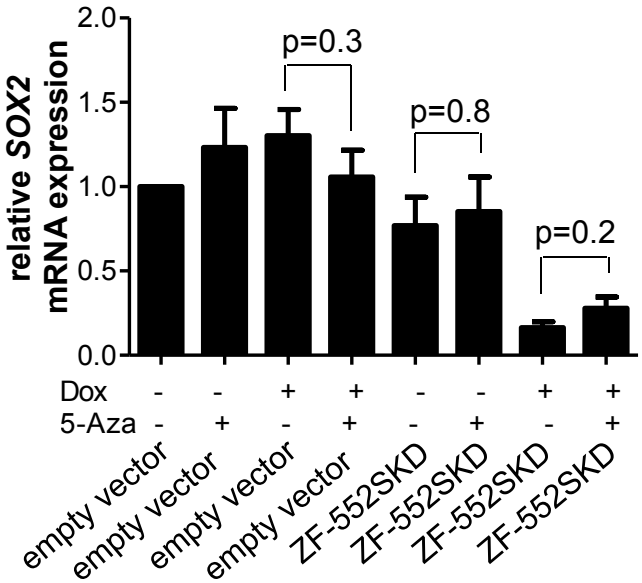
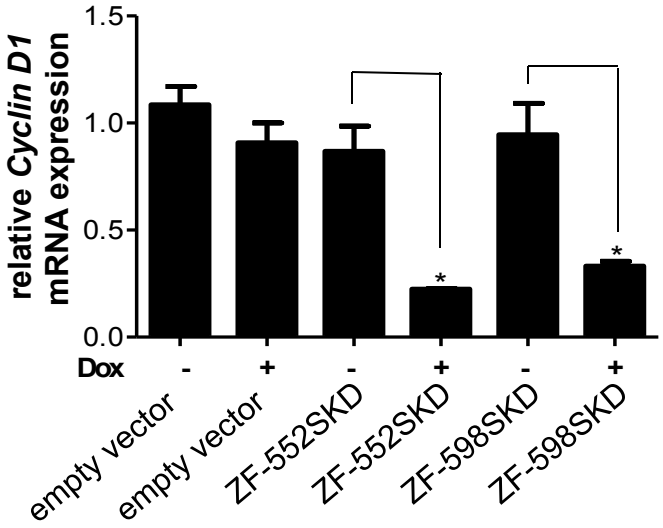


Supplemental Figure 2



Supplemental Figure 3



Supplemental Figure 4